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Application Serial No: 09/980,839
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TECH CENTER 1600/2900

IN THE CLAIMS:

This listing of claims will replace all prior versions and listing of claims in the application.

1-20. (CANCELED)

21. (WITHDRAWN) A method for the early detection of a flaviviral infection comprising: detecting an NS1 nonstructural glycoprotein of a flavivirus in a biological sample by an immunological method using at least two antibodies,

wherein the biological sample is obtained at anytime throughout the duration of the clinical phase of the infection,

wherein the two antibodies may be identical or different,

wherein a first antibody, called a capture antibody, is either (1) a polyclonal antibody preselected by immunocapture on the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form, or (2) a mixture of purified anti-NS1 monoclonal antibodies preselected for their high affinity for the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form, and

wherein a second antibody, called a revelation antibody, is a polyclonal antibody directed against the NS1 protein in hexameric form or a mixture of monoclonal antibodies directed against an NS1 protein in hexameric form.

22. (WITHDRAWN) The method as claimed in claim 21, wherein the flaviviral infection is an infection of the dengue virus.

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23. (WITHDRAWN) The method as claimed in claim 21, wherein the first antibody is attached to a solid support and the second antibody is optionally conjugated to a label.

24. (WITHDRAWN) The method as claimed in claim 23, wherein if the second antibody is not conjugated to a label, binding of the second antibody to the NS1 protein attached to the solid support is detected with a third antibody conjugated to a label.

25. (WITHDRAWN) The detection method as claimed in claim 24, wherein the label conjugated to the third antibody is an enzyme.

26. (WITHDRAWN) The detection method as claimed in claim 25, wherein

(A) the first antibody is a mouse polyclonal antibody selected by immunocapture of the NS1 protein of the dengue virus, wherein the NS1 protein is in hexameric form, and

(B) the second antibody is a polyclonal antibody from a rabbit immunized with the NS1 protein of dengue virus serotype 1, wherein the NS1 protein is in hexameric form,

(C) the third antibody reveals binding of the second antibody to NS1 protein, and the third antibody is an antibody conjugated to peroxidase and directed against the second antibody.

27. (CURRENTLY AMENDED) A boxed set for the early diagnosis of a flaviviral infection, comprising:

(A) a first antibody, called a capture antibody, which is either (1) a polyclonal antibody preselected by immunocapture on the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form or (2) a mixture of purified anti-NS1 monoclonal

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antibodies preselected for their high affinity for the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form;

(B) a second antibody, called a revelation antibody, which is either (1) a polyclonal antibody directed against NS1 protein in hexameric form or (2) a mixture of monoclonal antibodies directed against a NS1 protein in hexameric form, wherein the revelation antibody is identifiable with a conjugated label;

(C) at least one positive control comprising an NS1 protein of a flavivirus, wherein the NS1 protein is in hexameric form; and,

(D) at least one negative control comprising a normal, uninfected human serum.

28. (PREVIOUSLY PRESENTED) The boxed set as claimed in claim 27, wherein the NS1 protein is obtained from a culture supernatant either from infected mammalian cells or from mammalian cells transfected with a recombinant plasmid comprising a gene for an NS1 protein of a flavivirus or a fragment of the gene or a fragment of the flaviviral genome, the fragments being capable of expressing all or part of the NS1 protein.

29. (PREVIOUSLY PRESENTED) The boxed set as claimed in claim 27, wherein the NS1 protein is from a dengue virus.

30. (PREVIOUSLY PRESENTED) The boxed set for the early diagnosis of a flaviviral infection as claimed in claim 28, wherein the recombinant plasmid was deposited with the Collection Nationale de Cultures et de Microorganismes under the number I-2220.

31. (CURRENTLY AMENDED) A method for purifying an NS1 protein of a flavivirus, wherein the NS1 protein is in hexameric form, from a culture supernatant

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either of infected mammalian cells or of mammalian cells transfected with a recombined plasmid, comprising:

(A) expressing the ~~[[NSI]]~~ NS1 protein or a fragment of the NS1 protein from an NS1 gene or a fragment of the flaviviral genome, wherein the fragments are capable of expressing the NS1 protein prior to the purification of the NS1 protein;

(B) treating the ~~[[NSI]]~~ NS1 protein with a precipitating agent;

(C) centrifuging the treated ~~[[NSI]]~~ NS1 protein; and,

(D) separating a soluble form of the NS1 protein from a microparticulate form of NS1 protein.

32. (WITHDRAWN) The method for purifying NS1 protein as claimed in claim 31, wherein the flavivirus is a dengue virus.

33. (WITHDRAWN) The method for purifying NS1 protein as claimed in claim 32, wherein the flavivirus is dengue virus serotype 1.

34. (WITHDRAWN) An immunogenic composition, comprising as the active principle, an NS1 protein of a flavivirus, wherein the NS1 protein is in hexameric form, optionally associated with other proteins, and at least one pharmaceutical vehicle.

35. (WITHDRAWN) The immunogenic composition as claimed in claim 34, wherein the composition further comprises at least one mixture of NS1 proteins in hexameric form of a dengue virus serotype.

36. (WITHDRAWN) A method for preparing an immunogenic composition capable of inducing the production of antibodies *in vivo* comprising combining an NS1 protein in hexameric form, or an NS1 protein expressed from a system for the expression of NS1 protein in hexameric form, with at least one pharmaceutical vehicle.

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37. (WITHDRAWN) A method for manufacturing a medicinal product capable of inducing passive immunization comprising producing at least one monoclonal anti-NS1 antibody having a high affinity for NS1 protein in hexameric form, purifying the monoclonal antibody, and modifying the monoclonal antibody by selecting for Fab fragments or humanizing the monoclonal antibody, wherein the hexameric form is nondegraded.

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38. (CURRENTLY AMENDED) A method for selecting, *in vitro*, specific anti-NS1 antibodies able to diagnose an infection with a flavivirus, at an early stage, comprising binding the antibodies to NS1 protein in hexameric form, the hexameric form being nondegraded, and detecting the immune complex between the NS1 antibodies and the hexameric NS1 protein.

39. (WITHDRAWN) An immunogenic composition, comprising an active principle and a pharmaceutical vehicle, wherein the active principle is either a polynucleotide capable of expressing all or part of an NS1 protein of a dengue virus of any serotype, or the active principle is an expression system comprising at least one promoter capable of expressing, in a host into which it is injected, a DNA encoding an NS1 protein of a dengue virus of any serotype.

40. (WITHDRAWN) A method for expressing a polynucleotide encoding an NS1 protein of a dengue virus, comprising associating a polynucleotide of SEQ ID No. 1 with a promoter for said polynucleotide, and expressing the polynucleotide in a eukaryotic cell.

41. (NEW) The boxed set as claimed in claim 27, wherein the label is conjugated to the revelation antibody.

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42. (NEW) The boxed set as claimed in claim 27 further comprising a third antibody, wherein the label is conjugated to the third antibody and the third antibody binds to the revelation antibody.

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